Amendments to the drawings:

The attached sheet of drawings includes changes to Figure 9.

Attachment: Replacement Sheet

REMARKS

Applicants have amended the specification and claims to more particularly define the invention taking into consideration the outstanding Official Action. Page 1 of the specification has been amended to cross reference the provisional application benefit of which is claimed in the application data sheet which was filed with application on December 20, 2004. Since the claim for priority was contained in the Application Data Sheet as originally filed with the application, entry of the amendment and the specification in this regard is in order and is most respectfully request.

Applicants note the election with traverse and the Examiner's comments with respect to the reason for maintaining the restriction. Since it is believed that the present amendment will clearly establish of the patentability of claims 1-7, the restriction should be withdrawn upon an indication of allowance of these claims and corresponding method of use claims should be allowed in the present application.

The Examiner's comments with respect to the Information Disclosure Statement is noted. However, the information contained in the Information Disclosure Statement filed simply represents the information contained in the International Search Report and references should be with the file as transmitted with the International Search Report. For the convenience of the Examiner, additional copies are provided herewith along with a further copy of the form 1449 corresponding to that which was previously filed and therefore, since the references are of record, and were of record with respect to the international search, timely consideration of these references is now in order and is most respectfully requested.

The drawings with respect to Figure 9 have been corrected and a corrected sheet of drawings is submitted herewith. Accordingly, it is most respectfully requested that the objection to the drawings be withdrawn.

Applicants note the Examiner's comments with respect to the use of the trademark MILLIQ™and have amended the specification to provide the information concerning the trademark which relates to purified deionized water. This amendment

just serves for clarification and does not introduce new matter into the application as would be appreciated by one of ordinary skill in the art to which the invention pertains.

The rejection of claims 1-7 under 35 U.S.C. 112, second paragraph as being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicants regard as the invention has been carefully considered but is most respectfully traversed.

Claim 1 has been amended to provide a transitional phase including comprising which defines the scope of the invention which is now clearly recited and would be fully appreciated by one of ordinary skill in the art to which the invention pertains.

The comments with respect to claim 1 and the limitation "the coating" has been corrected to provide proper antecedent basis in the claim. Accordingly, it is most respectfully requested that this aspect of the rejection be withdrawn.

In addition, further amendments have been to the claims by clarifying that the coating on a metal surface is a mixed self-assembled monolayer of oligo(ethylene glycol)-terminated amide group-containing alkyl thiols and such thiols containing antigens bound via amide-group formation to the SAM-forming OEG molecule. This amendment is believed to clarify the claims and would be fully understood by one of ordinary skill in the art to which the invention pertains. One of ordinary skill in the art, in this context, would understand that by making the antigen coupling to the SAM forming molecule prior to forming the SAM of the mixture, controlled surface antigen density is obtained.

On page 3, lines 28-30 of the present specification it is disclosed that the antigens are synthetically bound to the OEG molecules prior to SAM formation by reacting functional groups on the antigens with functional groups terminating the OEG thiol. Further, on page 7, lines 7-10 is explained that a mixed monolayer was produced that contained two kinds of molecules, the first being protein repellent and the second being a TNT-analogue, thereby making it possible to obtain SAMs containing a varying amount of analogue that displays low levels of non-specific binding. It is of particular importance to be able to regulate the amount of bound antigen reversibly bound to an

antibody specific for an analyte antigen in displacement reactions, which is evident from, e.g., Figures 7 and 8, wherein Figure 7 shows that the mixture 99:1 detaches easily the bound antibody, whereas the mixtures 9:1 and 1:1 bind the antibodies too firmly to the surface for displacement reactions. Accordingly, it is most respectfully requested that the rejection of the claims as indefinite under 35 U.S.C. 112 be withdrawn.

Applicants most respectfully submit that all the claims now present in the application are in full compliance with 35 U.S.C. 112 and are clearly patentable over the references of record.

The rejection of claims 1, 2, 6 and 7 under 35 U.S.C. 103(a) as being unpatentable over Willner et al. (WO 00/43774, July 27, 2000) in view of Svedhem et al. and Bentley has been carefully considered but is most respectfully traversed.

The Willner reference discloses the formation of cystamine monolayer on a gold electrode (page 23, lines 14-24 and Fig. 4). As is evident from Fig. 4, the monolayer is first formed and thereafter the antigen is added so that an antigen-cystamine monolayer immobolized on the electrode is obtained (page 4, lines 2-3). In this Willner reference, there is no suggestion of any other "capturing agent" than cystamine, only a very non-specific mentioning of a sulfur containing moiety as the capturing agents is mentioned on page 14, lines 22-23. There is no discussion of any possible effects of the "capturing agent" in the Willner reference, and therefore there is no motivation for one of ordinary skill in the art to modify said "capturing agent".

The Svedhem reference (J. Org. Chem. 2001, 66, 4494-4503) discloses a formation of self-assembled monolayers (SAMs) on gold. Here is also discussed, as the Examiner has pointed out, self-assembled monolayer of oligo(ethylene glycol)-terminated (OEG) alkanethiol amides on gold. Svedhem states in the introduction that the SAMs provide well-defined planar biosensing surfaces for models studies of specific aspects of biomolecular recognition. Svedhem does not teach the preparation of oligo(ethylene glycol)-terminated amide group containing alkyl thiols containing antigens bound via amide-group formation to the OEG molecule prior to SAM-formation together

with oligo(ethylene glycol)-terminated amide group-containing alkyl thiols. Svedhem does not motivate one of ordinary skill in the art to make such mixed self-assembled monolayers, especially not containing antigens reversely bound to antiboides specific for the antigens which make the coated metal surface on a solid support according to Applicants present invention suitable for displacement reactions. Neither Svedhem et al. nor Willner et al. would motivate one of ordinary skill in the art to combine knowledge from these references and further develop the combined knowledge arriving at Applicants' presently claimed invention.

It is most respectfully submitted that the Examiner uses his own knowledge in stating that *the advantage* of having a structurally stable SAM, which has the characteristics of reducing nonspecific binding of proteins and other bioactive molecules *provides the motivation* to include the SAM of OEG-terminated alkanethiol amides of Svedhem et al. in the QCM biosensor of Willner et al. However, Applicants agree with the Examiner that it would have been obvious to one of ordinary skill in the art at the time of the invention to use conventional amide linkages formed between amine groups on drugs and ethylene glycol of OEG as taught by Bentley et al., but in Applicants present invention, the immobilization of antigens of interest is not on ready SAM of OEG-terminated alkanthiol amides of Svedhem et al. indicated by the Examiner, as explained above. The conventional chemistry is used prior to SAM formation.

By binding the antigens to the OEG thiols prior to the SAM formation together with OEG thiols it will be easy to control the amount of antigens, and subsequently antibodies specific for the analyte antigens, in the coating on a solid support. This is advantageous when the coating is used in displacement reactions. As already explained, it is evident from the present examples that the amount of antigens attached to antibodies in the coating effects the detection sensitivity of analyte antigens due to different binding capacity. Accordingly, it is most respectfully requested that this rejection be withdrawn.

The rejection of claims 3-5 under 35 U.S.C. 103(a) as being unpatentable over Willner et al. in view of Svedhem et al. and Bentley et al. as applied to claim 1 above

and further in view of Duffy has been carefully considered but is most respectfully traversed for the reasons discussed above. While Applicants appreciate that Duffy discloses arrays or patches for biomolecule binding, this reference does not disclose displacement reactions nor the formation of mixed molecules in the SAM. Accordingly, it does not overcome the deficiencies of the primary references and therefore it is most respectfully requested that this rejection be withdrawn.

In view of the above comments and further amendments to the specification, drawings and claims, favorable reconsideration and allowance of all the claims now present in the application are most respectfully requested.

Respectfully submitted,

BACON & THOMAS, PLLC

By Richard E Fichter
Richard E. Fichter
Registration No. 26,382

625 Slaters Lane - 4th Floor
Alexandria, Virginia 22314
Phone: (703) 683-0500
Facsimile: (703) 683-1080

REF:cjw
A02.wpd

DATE: October 30, 2006